IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Thomas ROTHMANN *et al.*	Confirmation No.: 1799
Appl. No. 10/586,785	Art Unit: 1797
Filed: March 16, 2007	Examiner: B. ETHERTON
For: **Contamination Barrier**	Atty. Docket No.: 00051-0031-001

Declaration of Dr. Thomas Rothmann Under 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

1. I, Dr. Thomas Rothmann, hereby declare and state as follows:

2. I am one of the named inventors of U.S. Application No. 10/586,785 (hereinafter "the '785 application"), filed March 16, 2007, entitled "Contamination Barrier." I am an also employee of the assignee of the '785 application, QIAGEN® GmbH.

3. I hold the degree of Doctor of Philosophy. A recent copy of my Curriculum Vitae, accurately listing my scientific credentials and work experience is attached herewith as Exhibit A.

4. I have read and understand claims 10-17 and 24-29, currently pending in the '785 application. I have also read and understand the Office Action, dated July 7, 2010.

5. Claims 10-17 and 24, of the '785 application have been rejected over Bloch *et al.*, U.S. Patent No. 5,411,876 in view of Rothmann *et al.*, Published U.S. Patent Application No. 2003/0065152 (hereinafter "Rothmann").

6. The Office Action asserts that Bloch allegedly discloses a method for improving the processing of polymerase chain reaction (PCR) solution by adding mineral

oil, waxes and greases to the surface as a barrier to both evaporation and contamination. However, the Office Action concedes that Bloch does not explicitly disclose that the contamination barrier prevents contamination during transfer of aqueous solutions and/or formation of aqueous aerosols, while also allowing for removal and processing of the aqueous solutions under the contamination barrier, or that the barrier comprises branched or unbranched hydrocarbons having 6 to 16 carbon atoms. *See* Office Action at page 4, second paragraph. The Office Action attempts to cure this deficiency with the disclosure of Rothmann.

7. The Office Action contends that Rothmann discloses a method that prevents contamination during the separation and purification of biopolymers, such as nucleic-acid containing polymers. The Office Action suggests that Rothmann discloses adding a layer of an immiscible hydrocarbon on top of an aqueous solution of the biopolymer, and that mineral oil is particularly preferred for this use. The Office Action further contends that Rothmann discloses that hydrocarbons having 8 to 12 carbon atoms are suitable for this use. The Office Action concludes that it would have been obvious to modify the mineral oil barrier disclosed in Bloch and replace it with C_8 to C_{16} hydrocarbons as disclosed in Rothmann in order to prevent aerosol formation.

8. The disclosure of Bloch relies on the use of greases or waxes to create a overlay on the surface of a PCR product. *See* Bloch at columns 3-4. The Office Action suggests that it would have been obvious to substitute hydrocarbons having 8 to 12 carbon atoms, as disclosed in Rothmann, for the greases and waxes utilized in Bloch. However, Rothmann does not disclose "adding a layer of an immiscible hydrocarbon on top of an

aqueous solution of the biopolymer." *See* Office Action at page 4, third paragraph. Instead, Rothmann discloses "the addition of branched or unbranched hydrocarbons to the aqueous mixtures which are to be analyzed and which contain the biopolymers or biopolymers as one component." Rothmann at page 2, paragraph 11.

9. It is my opinion that the "addition of branched or unbranched hydrocarbons" to the mixtures (i.e., inclusion in the aqueous solutions *via mixing*) as disclosed in Rothmann is not the same as covering the aqueous solution with a contamination barrier as required in the presently claimed invention. (*See* also Rothmann at page 3, claim 1, "mixing an aqueous solution . . . with at least one hydrocarbon . . .) While Bloch may disclose the use of wax or grease overlays, there is no indication that the addition of branched or unbranched hydrocarbons to an aqueous mixture, as disclosed in Rothmann, would provide a sufficient "barrier against mixing of aqueous reagents segregated above and below the grease or wax layer," as in Bloch. *See* Bloch at column 4, lines 37-39.

10. Furthermore, there is no reasonable expectation that the addition of branched or unbranched hydrocarbons to the solutions of Bloch would provide a sufficient barrier against mixing, which is a specific requirement of Bloch. The use of the branched or unbranched hydrocarbons in Rothmann to "allow elution to be carried out as completely as possible with reproducible elution volumes to avoid the contamination of other samples with fluids for analysis," provides no indication that these same hydrocarbons could function as barriers as required in Bloch.

11. There also would not have been a reasonable expectation of success that substituting the hydrocarbons disclosed in Rothman for the grease or wax overlay would

produce a covering that prevents contamination during transfer of aqueous solutions, and the covering prevents formation of aqueous aerosols, while allowing for removal and processing of said aqueous solutions under the contamination barrier without contamination from the contamination barrier, as required in the presently claimed invention.

12. The presently claimed invention indicates that the contamination barrier prevents contamination during transfer of aqueous solutions, and prevents formation of aqueous aerosols, while allowing for removal and processing of the aqueous solutions without contamination from the contamination barrier. Bloch teaches away from the use of liquid-phase oil overlays to achieve these goals, and instead would have directed those working in the field toward the use of solid-phase greases or waxes.

13. As disclosed in Bloch, "[t]he mineral oil overlay introduces several practical problems: (a) mineral oil contamination of reaction mixture samples withdrawn for post-PCR analysis . . . ." Bloch at column 3, lines 41-44. Thus, Bloch indicates that mineral oil overlays are not desirable as contamination barriers as these oils cause contamination of samples withdrawn for post-PCR analysis, i.e., they are not desirable for removal and processing of PCR solutions without contamination from the contamination barrier, as claimed. Rather, Bloch directs one to "replace the mineral oil overlay with a layer of grease or wax, the solidity of which at room temperature or below creates a barrier." Bloch at column 4, lines 35-40. Bloch further states that "wax, unlike oil, does not cling to the piper [sic] used to withdraw PCR product after amplification and, therefore, does not contaminate post PCR-detection reactions." Bloch at column 8, lines 25-31.

14. Therefore, it is my opinion that a technician working in the field at the time of filing this application would not have had a reasonable expectation of success with respect to the substitution of a liquid-phase hydrocarbon (i.e., hydrocarbons of from 6 to 16 carbon atoms as utilized in the presently claimed invention) for the solid-phase waxes and greases disclosed in Bloch to not only prevent contamination during transfer of aqueous solutions and prevent formation of aqueous aerosols; but also to allow for removal and processing of the aqueous solutions without contamination from the contamination barrier.

15. Rather, I believe that a technician in the field at the time of filing this application would have found it to be a surprising and unexpected result of the presently claimed invention that a contamination barrier comprising at least one water immiscible hydrocarbon or hydrocarbon mixture comprising branched or unbranched hydrocarbons of from 6 to 16 carbon atoms would prevent contamination during transfer of aqueous solutions, and also prevent formation of aqueous aerosols, while allowing for removal and processing of the aqueous solutions under the contamination barrier without contamination from the contamination barrier.

16. Thus, the presently claimed methods clearly display unexpected and surprising results, as compared to standard methodology known at the time of filing the present application.

17. I further state that all statements made on my own knowledge are true and that all statements made on information and belief are believed to be true and further that willful false statements and the like are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the U.S. Code and may jeopardize the validity of the application or any patent issuing thereon.

07/05/2011
Date

Dr. Thomas Rothmann

Curriculum Vitae

Personal Status

Name:	Thomas Rothmann
Nationality:	German, born November 20th, 1967
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Residence:	Zum Bräuhaus 15b, 40764 Langenfeld
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Education

1987-1993	Study of Biology at the Technical University of Darmstadt (Germany) and University of East Anglia (United Kingdom), Diploma Thesis in Molecular Biology/Virology: „Transcriptional regulation of the HPV-16 promoter/enhancer by p53"
since 1990	Member of the german national scholarship foundation
1993-1996	PhD with highest honor at the Institute of Applied Tumor Virology, German National Cancer Institute, Laboratory of Prof. Dr. Harald zur Hausen, Heidelberg and Technical University Darmstadt: „Heartmuscle specific gene therapy by adenoviral vectors"
1996-1998	Postdoctoral Fellow at the Institute of Applied Tumor Virology, German National Cancer Center, Laboratory of Prof. Dr. Harald zur Hausen, Heidelberg: Oncolytic Anti-Tumor-Viruses

Professional Experience

1998-2001	Scientist R&D, QIAGEN GmbH • Development of automated applications for BioRobot Product family
2001-2004	Senior Scientist R&D, QIAGEN GmbH • Project Manager of BioRobot MDx and Systems Integration Group Manager for OEM Project with large international diagnostic company
2005-2007	Associate Director R&D, QIAGEN GmbH • Projectmanager of OEM Instrument/Reagent Project with large diagnostic company (leading to FDA clinical trial) • Projectmanager of Tissue Disruption Portfolio • Setup and Head of Application group for QIAGEN Instrument Portfolio (customized solutions)
2008- 2010	Director R&D, QIAGEN GmbH • Setup and Head of Integrated Microsystems group with the focus to develop systems for „Point of Care" applications (Instrument, Reagents, Plastics, Microfluidics) • Since January 2010 Director Research NA, QIAGEN Sciences in Gaithersburg, USA (Expatriate Assignment) and Member of Womans Health Portfolio Team
2011 – present	Senior Director R&D, QIAGEN Sciences NA • Head of Assay Development & RD Services (supervising the functional groups Hybrid Capture Assay Development,

Isothermal Assay Development, RT-PCR Assay Development, BioBank, Laboratory Management and Analytical Chemistry) and Member of Prevention Portfolio Team.

Interests
Support of boy scouts, mentoring summer camps, understanding life

Potomac July 7th, 2011